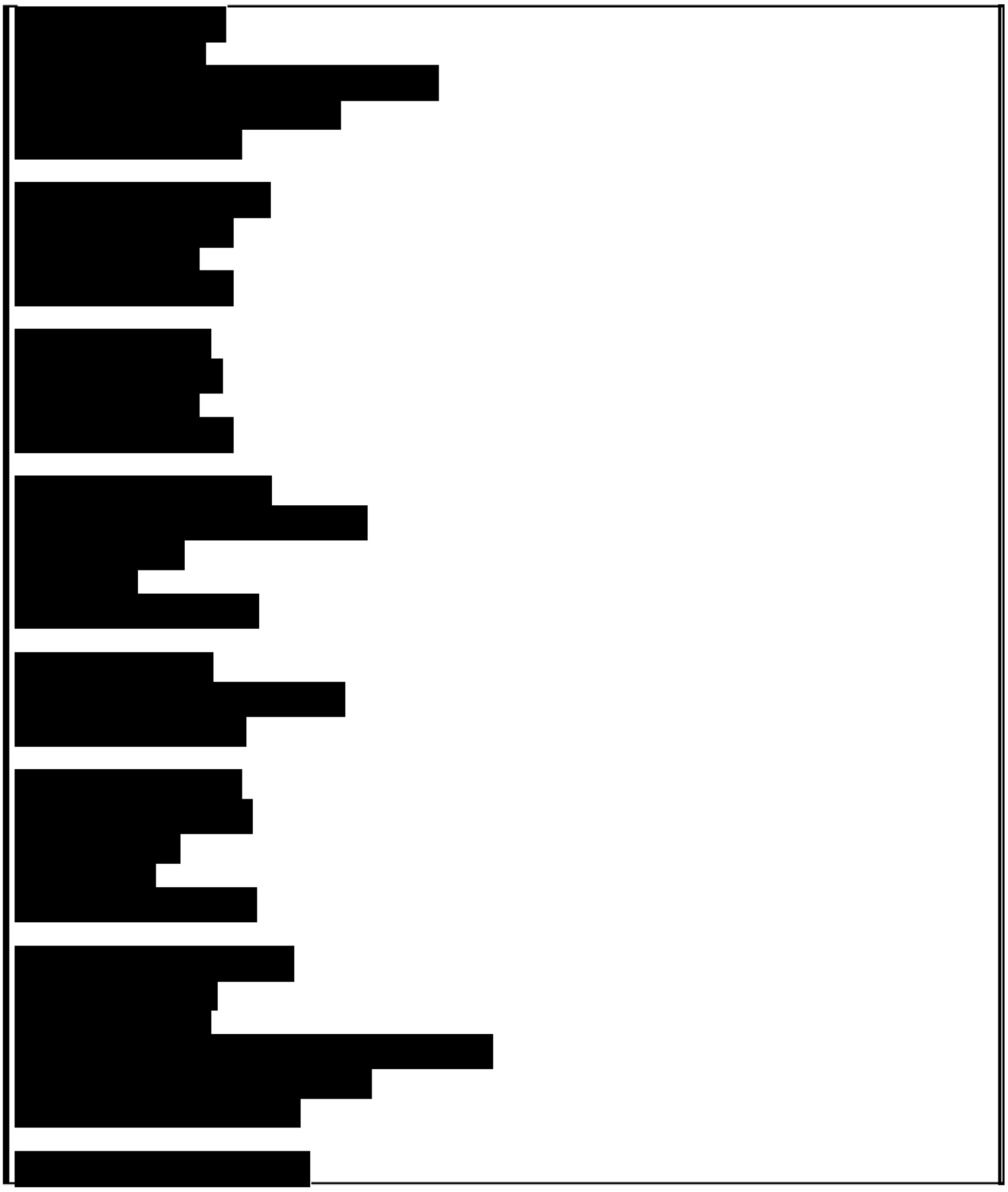
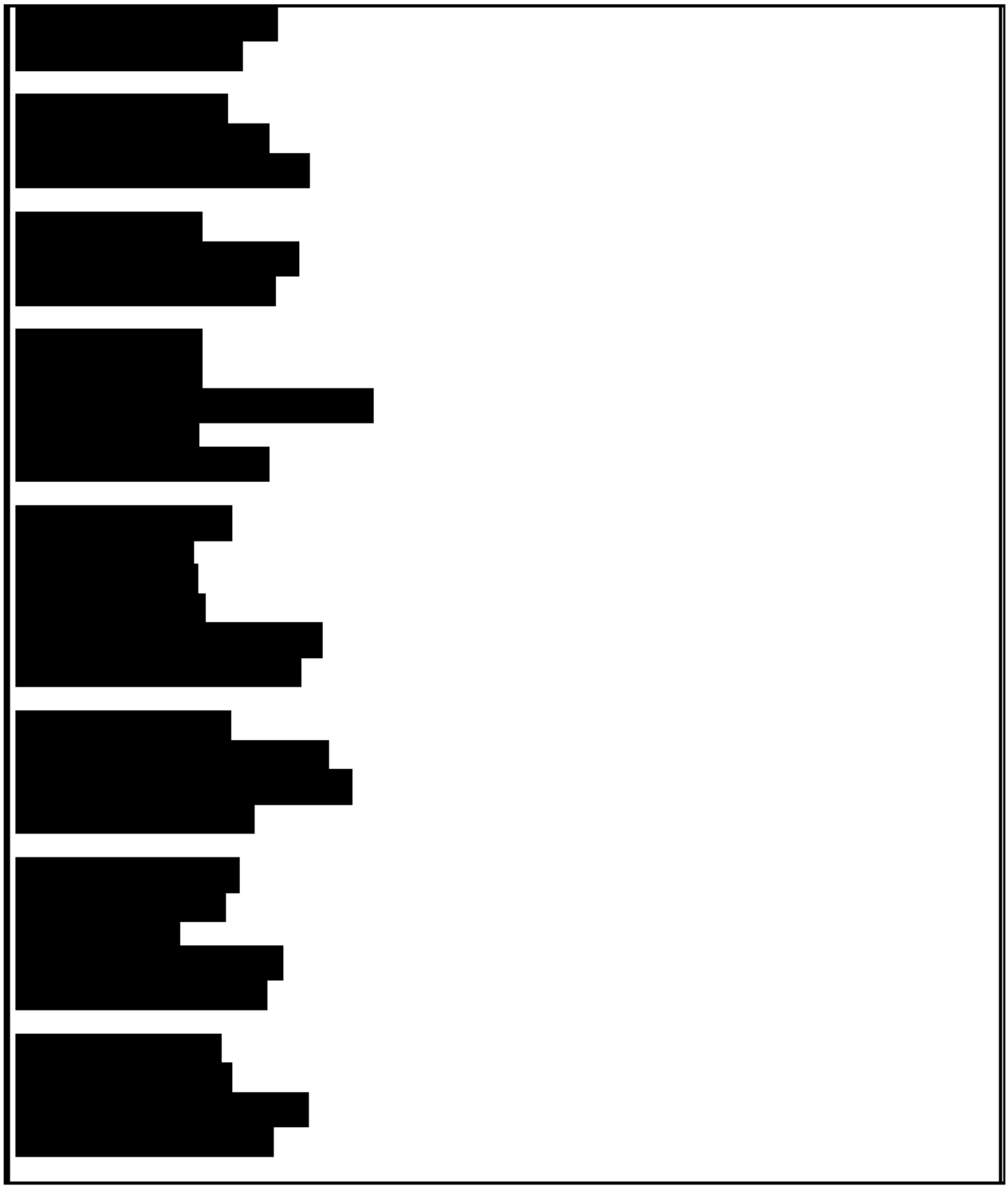
2 SYNOPSIS

Name of Sponsor/Company: Lundbeck Canada Inc	Individual Study Table Referring to Part of the Dossier	(For National Authority Use only)
Name of Finished Product: Trintellix®	Volume:	
Name of Active Ingredient: Vortioxetine	Page:	
Title of Study: Interventional, Open-Label, Single Cohort, Canadian Study to Describe the Relationship between Cognitive Symptoms and Work Productivity in Working Adults Treated with Vortioxetine for Major Depressive Disorder		
Investigators and Sub-Investigators: [redacted]		





Study centre(s): 26 Canadian sites contributed to patient recruitment and data collection

Publication (reference): Not applicable

Studied period (years): 2 years, 5 months (date of first enrolment): 05-Feb-2015 (FPFV) (date of last completed): 06-Jul-2017 (LPLV)	Phase of development: IV

Objective(s)

Primary objective:

- To describe the association/correlation between change from Baseline to Week 12 in patient-reported cognitive symptoms (PDQ-D-20) and the Work Limitations Questionnaire (WLQ) productivity loss score in gainfully employed patients receiving vortioxetine for a Major Depressive Episode (MDE)

Secondary objectives:

- To describe the following outcomes for patients receiving vortioxetine for a MDE at 12 and 52 weeks:
    a. Change in cognitive symptoms and performance (PDQ-D-20, DSST);
    b. Change in symptom and disease severity (QIDS-SR, CGI-I, CGI-S);
    c. Change in functioning and work productivity (WLQ productivity loss score, SDS, WPAI-Percent Overall Work Impairment, 12-item WHODAS 2.0);
    d. Treatment response rate, defined as a change in QIDS-SR of 50% or more from Baseline;
    e. Remission rate, defined as a QIDS-SR total score of ≤ 5.
- To describe and compare the following outcomes in first treatment and switch patients at 12 and 52 weeks:
    a. Change in cognitive symptoms and performance (PDQ-D-20, DSST);
    b. Change in symptom and disease severity (QIDS-SR, CGI-I, CGI-S);
    c. Change in functioning and work productivity (WLQ productivity loss score, SDS, WPAI-Percent Overall Work Impairment, 12-item WHODAS 2.0);
    d. Treatment response rate, defined as a change in QIDS-SR of 50% or more, from Baseline at 12 and 52 weeks;
    e. Remission rate, defined as a QIDS-SR total score of ≤ 5, at 12 and 52 weeks.
- To describe the association/correlation at Baseline, Week 12 and Week 52, for the following parameters:
    a. Cognitive symptoms and performance (PDQ-D-20*, DSST);
    b. Symptom and disease severity (QIDS-SR, CGI-I, CGI-S);

c. Functioning / work productivity (WLQ productivity loss score *, SDS, WPAI-Percent Overall Work Impairment, 12-item WHODAS 2.0).

- To describe and compare the association/correlation at Baseline, Week 12 and Week 52, in first treatment and switch patients, for the following parameters:
  a. Cognitive symptoms and performance (PDQ-D-20, DSST);
  b. Symptom and disease severity (QIDS-SR, CGI-I, CGI-S);
  c. Functioning / work productivity (WLQ productivity loss score, SDS, WPAI-Percent Overall Work Impairment, 12-item WHODAS 2.0).
- To describe the pharmaco-economic parameters of the whole cohort, as well as in first treatment and switch patients receiving treatment with vortioxetine for a MDE.

Exploratory objectives:

- To describe relationship and impact of anxiety symptoms (GAD-7) on cognitive symptoms and performance (PDQ-D-20, DSST), symptom and disease severity (QIDS-SR, CGI-I, CGI-S); and work productivity (WLQ productivity loss score, SDS, WPAI-Percent Overall Work Impairment, 12-item WHODAS 2.0).
- To identify predictors of change in cognitive symptoms and performance (PDQ-D-20, DSST), symptom and disease severity (QIDS-SR, CGI-I, CGI-S), work productivity (WLQ productivity loss score, SDS, WPAI-Percent Overall Work Impairment, 12-item WHODAS 2.0), among patient parameters (demographics, comorbidity, concomitant medication use, behavioural factors including smoking and alcohol or drug use), and disease parameters (duration, severity, prior treatments).

Safety objective:

- To describe the safety and tolerability of vortioxetine in a real-world setting.

**The association/correlation between change in PDQ-D-20 and WLQ productivity loss score from Baseline to 12 weeks, in the full study population, will be assessed as part of the primary objective.*

Methodology:
Design and population

This was an interventional, Canadian, multi-site, open-label, single cohort, flexible-dose study in patients diagnosed with an MDE who had not been treated with another antidepressant for the current episode (first treatment patients) and patients that required a switch from their current antidepressant due to inadequate response as per the judgement of the investigator (switch patients). All patients were treated with vortioxetine at the doses determined appropriate by the investigator. More specifically, the starting and recommended dose of vortioxetine was 10 mg once daily, depending on individual patient response, the dose may have been increased to a

maximum of 20 mg daily. After a dose increase, the dose may have been decreased back to 10 mg for tolerability reasons. Patients unable to tolerate at least a 10 mg dose were withdrawn from study.

The study was conducted in such a way as to emulate, as close as possible, a naturalistic real-world setting. In order to better represent the real-life routine care setting structured investigator-administered interventions and interviews that fall outside real-world practice were to be minimized. The total study duration from Baseline to the end of follow-up was approximately 56 weeks. Patients were assessed at Baseline, 4, 8, 12, 26, 39, 52 and 56 weeks. The study consisted of a 52-week treatment period with vortioxetine with a final safety follow-up visit at 56 weeks.

Number of patients (planned and analysed):

A total of 200 patients (100 patients diagnosed with a MDE who had not been treated with another antidepressant for the current episode (first treatment patients) and 100 patients that required a switch from their current antidepressant due to inadequate response as per the judgment of the investigator (switch patients)) were initially planned to be recruited by either primary-care physicians or psychiatrists across Canada. There were 26 sites that screened 267 patients and enrolled a total of 219 patients in the study.

Diagnosis and main criteria for inclusion:

This study enrolled adult patients diagnosed with MDD according to the Diagnostic and Statistical Manual of Mental Disorders, 5th Edition (DSM-5™) classification code 296.3x. Patients were classified as those who were to be treated with vortioxetine for a current MDE either as a first-choice antidepressant (first treatment patients) or switched to vortioxetine due to inadequate response to current antidepressant medication (switch patients), i.e. patients with MDD who in the opinion of the investigator have had an inadequate response to treatment with their current antidepressant at labelled doses for at least 6 weeks, where in the opinion of the investigator a treatment course with another antidepressant was warranted. Antidepressant switch could have been made abruptly with the last dose of current antidepressant taken no later than on the day of the Baseline visit and not more than 2 weeks prior to the Baseline visit. For patients switched from paroxetine, the last dose was to be taken no less than 1 week prior to the Baseline visit. In order to avoid too abrupt discontinuation for patients switching from high doses of antidepressant, the investigators were invited to gradually decrease the dose within the week prior to the Baseline Visit to reach the minimum therapeutic dose at Baseline.

Patients who met each of the inclusion criteria and none of the exclusion criteria were eligible to participate in this study.

Inclusion Criteria:

- The patient was able to read, understand and has signed the informed consent form.

- The patient was willing and able to attend study appointments within the specified time windows.
- The patient was a man or woman, aged ≥18 years and <65 years (In the Province of British Columbia, the patient must had been aged 19 years or older in order to give informed consent).
- The patient had been engaged in volunteer work or gainful employment (at least 20 hours per week) or was enrolled full-time in post-secondary studies or vocational training.
- The patient was an outpatient consulting a primary care physician or a psychiatrist.
- Patients must have had a diagnosis of MDD according to the Diagnostic and Statistical Manual of Mental Disorders, 5th Edition (DSM-5^{TM}) classification code 296.3x.
- The current MDE had been confirmed by the investigator.
- The patient's current MDE had not been treated with any antidepressant or the patient, in the opinion of the investigator, had an inadequate response to treatment with their current antidepressant at labelled doses for at least 6 weeks.
- The reported duration of the current MDE was at least 3 months.
- The patient had a Baseline score ≥15 on the QIDS-SR.
- The patient reported at least a minimal level of cognitive symptoms as defined by Baseline score of ≥30 on the PDQ-D-20.
- The patient was capable of communicating with the site personnel and was able to conduct the digit-symbol substitution test (DSST).
- The patient, if a woman, must have had agreed not to try to become pregnant during the study, AND:
    - Used adequate, highly effective contraception (defined as those that result in a low failure rate [that is, <1% per year] when used consistently and correctly, for example, implants, injectables, combined oral contraceptives, some intrauterine devices, sexual abstinence, vasectomized partner), OR;
    - Have had her last natural menstruation ≥24 months prior to the Screening/Baseline Visit, OR;
    - Have been surgically sterilized prior to the Screening/Baseline Visit, OR;
    - Have had a hysterectomy prior to Screening/Baseline Visit.

Exclusion Criteria:

- The patient score was >69 on the DSST at Screening/Baseline.
- The patient had previously been enrolled in this study, or any study to assess cognitive functioning, or any other study involving an investigational medication within the last 30 days.
- The patient was a member of the study personnel or of their immediate families, or was a subordinate (or immediate family member of a subordinate) to any of the study personnel.

- The patient was, in the opinion of the investigator, not able to complete all the study assessments including, but not limited to, patient-reported assessments and the DSST.
- The patient was pregnant or breast-feeding.
- The patient had a history of severe drug allergy or hypersensitivity, or known hypersensitivity to any of the excipients of the Investigational Medicinal Product (IMP).
- The patient had a current diagnosis or history of manic or hypomanic episode, schizophrenia or any other psychotic disorder, including major depression with psychotic features.
- The patient had physical, cognitive, or language impairment of such severity as to adversely affect the validity of the data derived from the patient reported outcomes (PROs).
- The patient had at significant risk of suicide or had attempted suicide <6 months prior to the Screening/Baseline Visit, as per investigator judgment.
- The current depressive symptoms were considered by the investigator to have been resistant to two adequate antidepressant treatments of at least 6 weeks duration each at the maximum recommended dose (according to Canadian labelling).
- The patient was taking or had taken disallowed recent or concomitant medication or it had been anticipated that the patient will require treatment with at least one of the disallowed concomitant medications during the study.
- The patient had a disease or was taking medication that could, in the investigator's opinion, had interfered with the assessments of safety, tolerability, or efficacy, or had interfered with the assessments of safety, tolerability, or efficacy, or interfere with the conduct or interpretation of the study.
- The patient was, in the investigator's opinion, unlikely to comply with the protocol or was unsuitable for any reason.
- The patient had previously been exposed to vortioxetine.
- The patient had suffered from personality disorder, mental retardation, pervasive development disorder, attention-deficit hyperactivity disorder, organic mental disorders, or mental disorders due to a general medical condition (DSM-5 criteria).
- The patient had a diagnosis or recent history of alcohol or other substance abuse or dependence (excluding nicotine or caffeine) which in the investigator's opinion, could had interfered with the assessments of safety, tolerability, or efficacy of the study drug, or had interfered with the conduct or interpretation of the study.

Test product, dose and mode of administration:

All patients were treated with vortioxetine 10 mg yellow film-coated oral tablets supplied by Lundbeck at the doses determined appropriate by the investigator an in accordance to the product monograph. More specifically, the starting and recommended dose of vortioxetine was 10 mg once daily (one tablet of 10 mg taken orally); depending on individual patient response, the dose may have been increased to a maximum of 20 mg daily (2 tablets of 10 mg taken orally).

After a dose increase, the dose may have been decreased back to 10 mg for tolerability reasons. Patients who were unable to tolerate a minimum of 10 mg per day were withdrawn from the study.

Duration of treatment:

The study consisted of a 52-week treatment period with vortioxetine with a safety follow-up visit approximately 4 weeks after the completion/ withdrawal visit. More specifically, the treatment period consisted in an open label acute treatment period of 12 weeks (Period I) followed by a 40-week open label extension period (Period II).

The total study duration from Baseline to the end of follow-up was approximately 56 weeks.

Reference therapy, dose and mode of administration, batch number:
Not applicable

Criteria for evaluation:
Criteria for evaluation included efficacy and safety measures.

Efficacy:

The primary efficacy endpoint of the acute phase (Baseline to Week 12) was the association/correlation of the changes from Baseline to Week 12 in patient-reported cognitive symptoms (PDQ-D-20) and the WLQ productivity loss score.

The primary efficacy endpoint of the extension phase (Week 12 to Week 52) was the association/correlation of the changes from Baseline to Week 52 in patient-reported cognitive symptoms (PDQ-D-20) and the WLQ productivity loss score.

Secondary outcomes measures were:

- Association/correlation of the changes from Baseline to Week 12 and Week 52 in objective neuropsychological test monitoring cognitive symptoms (DSST) and the WLQ productivity loss score.
- Changes from Baseline to Week 12 and Week 52 in:
    - I. Cognitive symptoms and performance
        - Perceived Deficits Questionnaire (PDQ-D-20)
        - Digit-Symbol Substitution Test (DSST)
    - II. Symptoms and disease severity
        - Quick Inventory of Depressive Symptomatology (QIDS-SR)
        - Clinical Global Impression- Severity Index (CGI-S)

- Clinical Global Impression-Improvement Index (CGI-I)*

III. Functioning and work productivity
- Work Limitations Questionnaire (WLQ) productivity loss score
- Sheehan Disability Scale (SDS)
  - Work Productivity and Activity Impairment Scale (WPAI)-Percent Overall Work Impairment
- World Health Organization Disability Assessment Scale (12-item WHODAS 2.0)

IV. Treatment response: decrease in QIDS-SR of 50% or more

V. Remission: QIDS-SR total score of ≤ 5

- Association/correlation between the following parameters at Baseline and Week 12 and Week 52 for the following parameters:
  - PDQ-D-20
  - DSST
  - QIDS-SR
  - CGI-S
  - WLQ productivity loss score
  - SDS
  - WPAI – Percent Overall Work Impairment
  - 12-item WHODAS 2.0
- Health Care Resource Utilization at Week 12, Week 39, Week 52 and cumulatively from Week 0 to Week 52.
  - Physician visits for MDD
  - Emergency Room visits for MDD
  - Hospitalization for MDD
  - Prescription and non-prescription medications used for MDD
  - Other health care services used for MDD
- Other Economic Parameters

- Number of days of work or school / other daily activities missed because of MDD
- Out of pocket expenses related to the patient's MDD
- Demographic information including age, sex, marital status, employment tenure, occupation, type of employer, educational attainment, income and race/ethnicity.
- Job type and description of work responsibilities and level

- Changes from Baseline to Week 12 and Week 52 in GAD-7.
- Association/correlation between GAD-7 and the following parameters at Baseline, 12 and 52 weeks as well as in changes from Baseline to Week 12 and to Week 52:
  - Cognitive symptoms and performance (PDQ-D-20, DSST)
  - Symptom and disease severity (QIDS-SR, CGI-I*, CGI-S)
  - Work productivity (WLQ productivity loss score, SDS, WPAI-Percent Overall Work Impairment, 12-item WHODAS 2.0)

Safety:

The following safety endpoints were assessed during the Acute and Extension Phases:

- Adverse events including serious and non-serious
- Reason for treatment discontinuation

**For CGI-I the actual score at the respective week were used rather than the change. CGI-I was not assessed at Baseline and thus, was excluded from the analyses involving Baseline.*

Statistical methods:

Analysis population:

- All Patients Treated Set (APTS) defined as all patients with a valid baseline assessment who took at least one dose of study medication was used to describe the patient disposition, the patient socio-demographics and baseline characteristics, vortioxetine exposure, and the safety endpoints.
- Full Analysis Set (FAS) defined as all patients from the APTS who attended at least one post-baseline study visit was used to describe the primary, secondary and exploratory endpoints, and treatment compliance.

- Per Protocol Set (PPS) defined as all patients in the FAS who had no major protocol deviations was used to describe the primary endpoint in addition to the FAS.

Descriptive statistics including the mean, median, standard deviation, and 95% confidence intervals (CI) of the mean for continuous parameters and frequency distributions (number and proportion) for categorical parameters were produced for all patient sociodemographics and baseline characteristics. Between-group (first treatment vs. switch group) differences were assessed for statistical significance with the Student's t-test for continuous variables and the Chi-Square statistic or the Fisher's exact test for categorical variables. Variables for which a trend for statistical significance ($P<0.15$) was observed and which were significantly associated with the respective outcome were considered as potential confounders and were included as covariates in the multivariable analyses.

Primary analyses:

The correlation between the change from Baseline to Week 12 in the PDQ-D-20 total score and the change from Baseline to Week 12 in the WLQ productivity loss score score was described by the partial correlation coefficient conditional on age, sex, Baseline PDQ-D-20, Baseline WLQ productivity loss score, disease duration and baseline disease severity (QIDS-SR, CGI-S).

Secondary analyses:

Summary statistics were produced for the changes from baseline to Week 12 and 52 in symptoms and performance (PDQ-D-20, DSST), symptom and disease severity (QIDS-SR, CGI-I, CGI-S) and functioning and work productivity (WLQ productivity loss score, SDS, WPAI-Percent Overall Work Impairment, 12-item WHODAS 2.0). Changes from baseline to Week 12 and 52 were assessed with the paired Student's t-test. The rate of response to treatment and remission were described as the proportion of patients with response and remission at 12 and 52 weeks of treatment and 95% confidence intervals around the estimate of these proportions were reported. These analyses were also stratified by first treatment and switch patient sub-groups. The sub-groups were compared with Student's t-test for independent samples and general linear models were used to adjust for the between-group differences in patient sociodemographic and baseline characteristics. Time to treatment response and remission were assessed with the log-rank text and Cox's proportional hazards models were used to adjust for between-group differences in patient sociodemographic and baseline characteristics.

Correlations at baseline, Week 12, and Week 52 were described with the Pearson Correlation for the following associations: Cognitive symptoms and performance (PDQ-D-20, DSST), symptom and disease severity (QIDS-SR, CGI-I and CGI-S), and functioning and work productivity (WLQ productivity loss score, SDS, WPAI-Percent Overall Work Impairment, 12-item WHODAS 2.0). These analyses were also stratified by first treatment and switch patient

sub-groups. The between group differences were assessed with the t-test for correlation coefficients.

Summary statistics were produced for the whole cohort, as well as in first treatment and switch patients for the pharmaco-economic parameters.

Exploratory analyses:

Pearson Correlation and General Linear Models were used to assess the relationship between anxiety symptoms (GAD-7) and each of the following parameters (i) at baseline, (ii) week 12, (iii) week 52, (iv) in the change from baseline to week 12, (v) in the change from baseline to week 52: cognitive symptoms (PDQ-D-20, DSST), symptom and disease severity (QIDS-SR, CGI-I, CGI-S) and work productivity (WLQ productivity loss score, SDS, WPAI-Percent Overall Work Impairment, 12-item WHODAS 2.0).

To identify predictors of change from baseline to week 52 in cognitive symptoms (PDQ-D-20, DSST) and performance, severity of symptoms of depression (QIDS-SR, CGI-I, CGI-S), and work productivity (WLQ productivity loss score, SDS, WPAI-Percent Overall Work Impairment, 12-item WHODAS 2.0), bivariate analyses and multivariate General Linear Models with stepwise variable selection were used.

Safety analyses:

Safety and tolerability was evaluated with the total number of adverse events (AEs), the total number and proportion of subjects experiencing at least one AE overall and within each system organ class and preferred term. AEs were classified according to the MedDRA dictionary of terms (Version 20.1. To count the number of subjects who experienced each AE, subjects experiencing the same AE multiple times was only counted once for the corresponding system organ class and body system. In addition, an overview of all AEs was summarized using the total number of AEs, the total number and percentage of patients who experienced an AE according to severity (mild, moderate, severe), seriousness (serious, non-serious, or lack of drug effect*), relation to study drug (not related, possible, probable), overdose, overdose type, action taken and outcome (recovered, recovering, recovered with sequelae, not recovered, death).

Adverse events were classified according to the time of onset of the adverse event:

- Pre-treatment adverse event – an adverse event that started on or after the date the patient signed the Informed Consent Form and prior to the date of first dose of IMP.
- Treatment-emergent adverse event (TEAE) – an adverse event that started or increased in intensity on or after the date of first dose of IMP until the completion visit.

In addition, similar tables were produced for:

- All TEAEs possibly/probably related to the study drug
- Serious TEAEs

- TEAEs leading to study drug discontinuation

* While the lack of drug effect is not considered an adverse event, the information is included for reporting purposes

SUMMARY – CONCLUSIONS

EFFICACY RESULTS:

The primary efficacy analysis evaluated the correlation between the change from Baseline to Week 12. A statistically significant, positive and strong correlation between the change in PDQ-D-20 and the WLQ productivity loss score was observed at Week 12 for the FAS (r=0.606, P<0.001). Strong correlation between PDQ-D-20 and WLQ productivity loss was observed among First Treatment patients (r=0.676; P<0.001), though moderate correlation was shown for Switch patients (r=0.515, P<0.001). Between-group differences showed that higher correlation was observed for First Treatment vs. Switch patients approaching statistical significance (P=0.125). At Week 52, statistically significant, positive and strong correlation was reported for the FAS (r=0.731, P<0.001), First Treatment patients (r=0.710, P<0.001), and Switch patients (r=0.788, P<0.001). Similar findings were observed for the partial correlation coefficient between the change from Baseline in PDQ-D-20 and in WLQ productivity loss score using the LOCF method.

Despite the correlation between changes in subjective cognitive symptoms (PDQ-D-20) and work productivity (WLQ productivity loss) found in the current study, only a weak correlation between changes in objective cognitive performance (DSST) and work functioning (WLQ productivity loss) was observed for the FAS population at Week 12 and Week 52. The findings for First Treatment patients (r = -0.327), and Switch patients (r = -0.197) were also weakly correlated.

After 12 Weeks of treatment with vortioxetine, patients showed significant improvements in perceived cognitive symptoms and cognitive performance (as shown by PDQ-D-20 and DSST, respectively), symptoms and disease severity (as shown by QIDS, CGI-S), work productivity (as shown by WLQ productivity loss score and WPAI-Percent Overall Work Impairment), and functioning (as shown by SDS and WHODAS) among the FAS, First Treatment and Switch patients. Furthermore, after 52 Weeks of treatment, continued significant improvements were noted for all assessments.

The proportion of patients achieving treatment response for the FAS at Week 12 was 62.7% and increased to 77.1% at Week 52. Stratified by First Treatment vs. Switch groups, treatment response was comparable at Week 12 (62.2% vs. 63.2%). Though, at Week 52, the treatment response was found to be slightly higher among the Switch subgroup (83.3% vs. 71.0%).

Remission was achieved for the FAS at Week 12 by 33.3% of patients and increased to 55.7% at Week 52. Stratified by First Treatment vs. Switch groups, remission was comparable at Week

12 (28.9% vs. 37.9%). Though statistical between group differences were observed at Week 52, with remission being higher among the Switch patients (66.7% vs. 45.2%, P=0.017).

In general, out-of-pocket expenses generally decreased to Week 52, as did rates of HCU for all parameters assessed. The only significant between-group difference was the cumulative (all time points combined) out-of-pocket expense for prescription medication being higher for Switch vs. First Treatment patients (77.9 CAD vs. 15.1 CAD; P=0.002). With respect to employment, the proportion patients steadily decreased over time, as did the proportion of full-time employment. Among the FAS, missed work due to depression decreased over time without any differences between First Treatment and Switch patients.

SAFETY RESULTS:

A total of 530 AEs were reported by 157 (71.7%) patients within the APTS Population; 508 AEs were considered treatment-emergent and 7 AEs were considered pre-treatment. 69.4% of AEs were non-serious and 5.0% of AEs were serious. Most AEs were of mild (53%) and moderate (48%) severity. The majority of AEs did not require action be taken. Drug discontinuation was reported for 19.2% of patients, with dose adjustments performed in 6.8%.

By SOC and PT, the profile of treatment-emergent adverse events (TEAEs) reported for the current study is in agreement with the Product Monograph for vortioxetine: the most common reported PTs were nausea (29.2%), headache (11.9%), followed by insomnia, nasopharyngitis and anxiety (9.1%, 6.8%, and 6.4%, respectively). Serious TEAEs were most commonly reported for the SOC "Psychiatric disorders" (2.3% of patients), which included serious TEAEs of suicidal ideation (1.4%, n=3), depression suicidal (0.5%, n=1), and depressive symptom (0.5%, n=1). With the exception of suicidal ideation (reported by 3 patients), all other serious TEAEs were reported by one patient.

No deaths were reported during the course of the study. Overall, vortioxetine was found to be safe and tolerable for the management of major depressive disorder in real-world clinical practice, with no new safety signal detected.

CONCLUSION:

This study assessed the effectiveness and safety of vortioxetine for the treatment of MDD in a real-world clinical setting. The results of this study indicate that vortioxetine is effective for the treatment of MDD in real-world clinical practice, showing positive improvements in depression severity, cognitive function, overall function, as well as improved workplace productivity. Furthermore, both first treatment and switch patients showed significant improvements in these parameters. In addition, vortioxetine was found to be safe and well tolerated, as the profile of AEs reported is in agreement with the Product Monograph, and no new safety signal was

detected. Furthermore, vortioxetine was found to reduce health care resource use and out-of-pocket expenses.